Remarks

Claims 1-9 and 11-13 are pending. Claims 1, 2, 4-9, and 11-13 have been amended. Claims 3, 10 and 27-37 have been canceled. Support for the amendment to claim 1 (separation of ligand mixture) can be found, for example, at pages 28-31 (Example 3) and in the dependent claims. Support for the amendment to claim 4 (two-dimensional gel) can be found, for example, at pages 28-31. Claim 12 has been amended to clarify that all of the ligands are unknown. Claims 2-9 and 11-13 were amended to properly depend from claim 1.

The present invention is directed to novel methods aimed at producing arrays of anti-ligands for the purposes of detecting ligand/anti-ligand binding/interaction.

Rejection Under 35 U.S.C. § 112, first paragraph

Claims 1-9 and 11-13 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The Examiner is respectfully reminded that both the written description and enablement requirements are defined by 35 U.S.C. § 112, first paragraph, which states that the patent specification must contain "a written description of the invention, and of the manner and process of making and using it...[such] as to enable any person of ordinary skill in the art to which it pertains ... to make and use the same ... " The purpose of the written description requirement is

to prevent a patentee from later asserting that he invented something which he did not. Thus the patentee must "recount his invention in such detail that his future claims can be determined to be encompassed within his original creation." *Vas- Cath Inc. v. Mahurkar*, 935 F.2d 1555, 1561, 19 U.S.P.Q.2d 1111, 1115 (Fed. Cit 1991).

Claim 1 has been amended to require the separation of ligands before exposure to the anti-ligand library. Such separation may be accomplished using methods such as size exclusion chromatography, gel electrophoresis, isoelectric focusing, or combinations thereof (i.e. 2-D electrophoresis (for example, see newly amended claim 4). The claimed methods are directed to a novel method to generate an anti-ligand array. One of ordinary skill in the art would clearly understand what is meant by the terms "ligands", "library" and "anti-ligand", in view of the present specification and technologies known at the time of filing the present application. Replicable units are clearly defined at page 9, lines 14-20. Furthermore, as stated at page 6, lines 21-24, "the identity of at least some, and preferably all, of the ligands and/or anti-ligands can be unknown. Hence, prior characterization of ligands, and/or anti-ligands is unnecessary.

Each of the terms that the Examiner has questioned is clearly described in the specification (for example, "replicable units", see page 9, lines 14-20; "ligands", see page 8, lines 22-26; "library", see page 23, lines 9-19; "anti-ligand", see page 6, lines 12-19 and lines 28-4, bridging pages 8 and 9; and "mixtures", see page 23, lines 21-26).

Rejection Under 35 U.S.C. § 112, second paragraph

Claims 1-9 and 11-13 were rejected under 35 U.S.C. § 112, second paragraph, as being indefinite. Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

The applicants respectfully submit that the term "variant or derivative" is clear in view of page 6, lines 12-19; page 11, lines 19-24; and page 13, lines 15-23. With regard to claim 11, the applicants submit that either the identity of the ligand or the anti-ligand is unknown or known, or both unknown or known. Each of claims 5, 7, 9, 11, and 12 have been amended and obviate the rejections made by the Examiner under this paragraph of 35 U.S.C. § 112.

Rejection Under 35 U.S.C. § 102

Claims 1-9 and 11-13 were rejected under 35 U.S.C. § 102(e), **or in the alternative, under 35 U.S.C. § 103(a)**, as being anticipated by U.S. Patent No. 6,329,209 to Wagner et al. ("Wagner"). Applicants respectfully traverse this rejection to the extent that it is applied to the claims as amended.

Wagner teaches a method for producing an array of protein-capture agents comprising the first step of selecting the protein-capture agents from a library herein these agents are selected by their affinity to bind to proteins. The second step of the method comprises producing a plurality of purified samples of the protein-capture agents selected in the first step. The third step comprises immobilizing the protein-capturing agents of each different purified sample onto a

substrate surface, giving rise to patches of the agents on discrete, known regions on the substrate surface.

Wagner teaches the immobilization of unknown proteins on a substrate surface without first separating the mixture of ligands before they are exposed to the library of anti-ligand molecules. This is in direct contrast to the presently claimed invention wherein ligands, especially unknown ligands, are separated prior to binding.

The applicants respectfully submit that a complex ligand mixture, such as a biological sample (for example, blood plasma) contains thousands of different proteins (ligands) at vastly different concentration levels, ranging from several milligram per milliliter down to a few molecules per milliliter. In many cases, the most abundant proteins are of less interest as they include mostly structural proteins and common metabolic enzymes or, in the case of blood plasma, transport proteins such as albumin.

Direct biopanning of anti-ligand-displaying phages using an unfractionated (unseparated) sample leads to an overwhelming bias towards selecting anti-ligands to the most abundant proteins. Furthermore, low abundant proteins occurring at nanomolar levels will be very difficult to isolate as the concentration is too low to obtain complex binding between ligand and anti-ligand. By separating/fractionating the sample protein prior to selection, the complexity of each fraction is reduced and the concentration of the individual ligands can be increased.

Claim Objections

Claims 7, 8 and 9 were objected to because lines were crowded together. This problem has been corrected.

Allowance of claims 1, 2, 4-9, and 11-13, as amended, is respectfully solicited.

Respectfully submitted,

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Certificate of Facsimile Transmission

I hereby certify that this Amendment and Response to Office Action, Petition for Revival of an Application for Patent Abandoned Unintentionally Under 37 CFR § 1.137(b), and any documents referred to as attached therein are being facsimile transmitted on this date, September 12, 2003, to the Commissioner for Patents, U.S. Patent and Trademark Office, P.O. Box 1450, Alexandria, VA 22313-1450.

Pam Turnbough

Pam Turnbough

Date: September 12, 2003

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